

We claim:

1. A compound of the formula:

$X_1-X_2-X_3$ -Leu- X_4 -Glu-Leu- X_5 - X_6 -Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn- X_7 - Z_3 [SEQ.ID.NO.27] wherein:

- 5 (a) X_1 is (i) a group of two amino acid residues selected from the group consisting of Leu-Leu, Val-Leu, Ile-Leu, tert-Leu-Leu, Nle-Leu, and Ala-Thr, and N-acylated derivatives thereof; or (ii) the group Z_1 -Ser-Thr- Z_2 -Val-Leu [SEQ.ID.NO. 28] wherein Z_1 is an
10 amino acid residue selected from the group consisting of Leu, Val, Ile, tert-Leu, Nva, Abu, and Nle or an N-acylated derivative thereof or Z_1 is an alkanoyl group; and
 Z_2 is a amino acid residue selected from the group
15 consisting of Ala, Ser, Cys, and Thr;
- (b) X_2 is an amino acid residue selected from the group consisting of Gly, Glu, Asn or Aib;
- (c) X_3 is an amino acid residue selected from the group consisting of Arg, Orn, Lys and e-amidated derivatives
20 thereof;
- (d) X_4 is a group of two amino acid residues selected from the group consisting of Ser-Gln, Thr-Gln, Ala-Asn and Thr-Asn;
- (e) X_5 is an amino acid residue selected from the group consisting of His, Aib, Ile, Leu and Val;
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- (f) X_6 is an amino acid residue selected from the group consisting of Arg, Orn and Lys and e-amidated derivatives thereof;
- (g) X_7 is a group having 6 amino acid residues selected

from the group consisting of

- (i) Thr-Gly-Ser-Asn-Thr-Tyr-NH₂ [SEQ.ID.NO. 29];
- (ii) Thr-Gly-Ser-Gly-Thr-Pro-NH₂ [SEQ.ID.NO. 30];
- (iii) Val-Gly-Ser-Asn-Thr-Tyr-NH₂ [SEQ.ID.NO. 31];
- 5 (iv) Val-Gly-Ser-Gly-Thr-Pro-NH₂ [SEQ.ID.NO. 32]; and

(h) Z₃ is OH or NH₂;

with the proviso that the compound does not have the
formula of any of SEQ. ID. NOS. 14 to 26;
and pharmaceutically acceptable salts thereof.

10 2. A compound according to claim 1 wherein Z₃ is
NH₂.

3. A compound according to claim 1 wherein X₂ is
Gly.

15 4. A compound according to claim 3 wherein X₅ is His
or Aib.

5. A compound according to claim 4 wherein X₄ is
Ser-Glu.

6. A compound according to claim 5 wherein X₇ is
Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 29] or Thr-Gly-Ser-Gly-
20 Thr-Pro-NH₂ [SEQ.ID.NO. 30].

7. A compound according to claim 6 wherein X₁ is Z₁-
Ser-Thr-Z₂-Val-Leu [SEQ.ID.NO.28].

8. A compound according to claim 7 wherein X₃ and X₆

are e-amidated with a carboxylic acid having 1 to 8 carbon atoms.

9. A compound according to claim 9 wherein Z_1 is an alkanoyl group having 1 to about 10 carbon atoms or Leu.

5 10. A compound according to claim 9 wherein Z_2 is Ala or Cys.

11. A compound according to claim 10 wherein Z_1 is an alkanoyl group.

10 12. A compound according to claim 11 wherein X_3 and X_6 are formamidated or acetamidated.

13. A compound according to claim 12 wherein Z_2 is Ala.

14. A compound according to claim 13 wherein X_3 and X_6 are Lys(For).

15 15. A compound according to claim 14 wherein Z_1 is 4-methylpentanoyl.

16. A compound according to claim 1 which has an amino acid sequence selected from the group consisting of:

20 Leu-Ser-Thr-Cys-Val-Leu-Gly-Arg-Leu-Ser-Gln-Glu-
Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-
Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 1];

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4-methylpentanoyl-Ser-Thr-Ala-Val-Leu-Aib-
Lys(For)-Leu-Ser-Gln-Glu-Leu-Aib-Lys(For)-Leu-
Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Gly-Thr-
Pro [SEQ.ID.NO. 2];

5 Ac-Leu-Ser-Thr-Ser-Val-Leu-Gly-Arg-Leu-Ser-Gln-
Glu-Leu His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-
Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 3];

Leu-Ser-Thr-Ala-Val-Leu-Gly-Arg-Leu-Ser-Gln-Glu-
Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-
Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 4];

Leu-Ser-Thr-Ser-Val-Leu-Gly-Arg-Leu-Ser-Gln-Glu-
Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-
Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 5];

15 Ac-Leu-Ser-Thr-Ala-Val-Leu-Gly-Arg-Leu-Ser-Gln-
Glu-Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-
Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 6];

Ac-Leu-Ser-Thr-Cys-Val-Leu-Gly-Arg-Leu-Ser-Gln-
Glu-Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-
Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 7];

20 Val-Leu-Aib-Lys(For)-Leu-Ser-Gln-Gl-Leu-Aib-
Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-
Ser-Asn-Thr-Tyr [SEQ.ID.NO. 8];

Ac-Val-Leu-Aib-Lys(For)-Leu-Ser-Gln-Glu-Leu-Aib-

Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 9];

4-methylpentanoyl-Ser-Thr-Ala-Val-Leu-Aib-Lys(For)-Leu-Ser-Gln-Glu-Leu-Aib-Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 10];

4-methylpentanoyl-Ser-Thr-Cys-Val-Leu-Aib-Lys(For)-Leu-Ser-Gln-Glu-Leu-Aib-Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 11];

Ala-Thr-Aib-Lys(For)-Leu-Ala-Asn-Glu-Leu-Aib-Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 12]; and

Ac-Ala-Thr-Aib-Lys(For)-Leu-Ala-Asn-Glu-Leu-Aib-Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 13].

17. The compound Leu-Ser-Thr-Cys-Val-Leu-Gly-Arg-Leu-Ser-Gln-Glu-Leu-His-Arg-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Asn-Thr-Tyr [SEQ.ID.NO. 1].

18. The compound 4-methylpentanoyl-Ser-Thr-Ala-Val-Leu-Aib-Lys(For)-Leu-Ser-Gln-Glu-Leu-Aib-Lys(For)-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Gly-Thr-Pro [SEQ.ID.NO. 2].

19. A composition comprising a compound of any of claims 1 to 18 in a pharmaceutically acceptable carrier.

20. A method of treating diabetes in a subject in need of treatment which comprises administering to said
5 subject a therapeutically effective amount of a compound of any of claims 1, 2, 15, 16, 17 or 18.

21. A method according to claim 20 wherein said diabetes is type I diabetes.

22. A method according to claim 20 wherein said
10 diabetes is type II diabetes.

23. A method of beneficially regulating gastrointestinal motility in a subject comprising administering to said subject a therapeutically effective amount of a compound of any of claims 1, 2, 15, 16, 17 or
15 18.

24. A method according to claim 23 wherein said beneficial regulation of gastrointestinal motility comprises delaying gastric emptying.

25. A method of treating a disorder selected from the
20 group consisting of: impaired glucose tolerance; postprandial hyperglycemia; obesity; and Syndrome x; in a subject in need of treatment which comprises

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administering to said subject a therapeutically effective amount of a compound of any of claims 1, 2, 15, 16, 17 or 18.

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